

## **REMARKS**

Upon entry of the foregoing amendment, Claims 1, 3-8, 10, 12-15, and 17-22 will remain pending in the application. Claims 2, 9, 11 and 16 have been canceled; Claims 1, 3-8, 10, 12-15, and 17-20 have been amended; and Claims 21-22 have been added. The amendments are supported by page 9, lines 1-4 (for Claim 15), and by original Claims 8 and 11 (for new Claims 21-22). These changes do not introduce new matter, and their entry is respectfully requested.

In the Office Action of May 6, 2008, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

### **Oath and Declaration**

The Examiner indicates that the oath or declaration is defective under 37 CFR 1.67(a) and 37 CFR 1.69(b). Applicant submits concurrently herewith declaration in the German language by an English translation together with a statement that the translation is accurate, as is required by 37 CFR 1.69(b).

### **Abstract**

The abstract stands objected to for not describing the invention in sufficient detail and for the presence of legal terminology. The abstract has been amended to address the Examiner's concerns.

**Claim Rejections Under 35 U.S.C. § 101**

Claims 1-14 stand rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter and a “use” is not a statutory class of invention. Claims 1, 2-8 and 10-14 have been amended to delete “use” and recite method steps. Claims 2 and 9 have been canceled. Applicant respectfully submits that the amendments obviate the ground of the rejection. Withdrawal of the rejection under 35 U.S.C. 101 is respectfully requested.

**Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-20 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that it is not clear what constitutes a “use” as is recited in claims 1-14. Claims 1-14 have been amended to recite a “method.”

The Examiner points out that Claims 7, 11, 19 and 20 are indefinite because of the phrase “in particular.” Claims 7, 19 and 20 have been amended to delete the phrase. Claim 11 has been canceled.

The Examiner states that Claims 10 and 17 are indefinite because of the conjunction “and/or.” Claims 10 and 17 have been amended to delete the conjunction.

The Examiner alleges that Claims 11 and 19 are indefinite because it is not clear if the molar ratio is referring to the ratio of the compound and the albumin as reactants, or to the ratio of the compound and the albumin in the conjugate product. Claim 19 has been amended to recite a ratio of the compound and the albumin as reactants. Claim 11 has been canceled.

The Examiner further alleges that the “a” in Claim 15 should be “the” and that there is no antecedent basis for “the protein” in Claim 20. Claims 15 and 20 have been amended to address the Examiner’s concerns.

In view of the foregoing, Applicant respectfully submits that the amendments obviate the grounds for the rejections. Withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is respectfully requested.

**Claim Rejections Under 35 U.S.C. § 102(b)**

Claims 1-18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Bures et al. Neoplasma, 35:329-342 (hereinafter “Bures”) for the reasons set forth on page 4 of the Office Action. Claims 1-18 also stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sutton et al. (hereinafter “Sutton”) (U.S. Patent No. 5,993,805) for the reasons set forth on page 5 of the Office Action. Applicant respectfully traverses the rejections.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In this case, independent Claim 1, as amended, is directed to a method for modulating a transplantation-associated immune response, comprising: administering to a subject in need an effective amount of a conjugate comprising a carboxyl group-containing organic compound and albumin, wherein said carboxyl group-containing organic compound is a cytostatic or an immunosuppressant.

Independent Claim 15, as amended, is directed to a method for preparing a conjugate comprising a carboxyl group-containing organic compound and albumin, said method comprising: activating said carboxyl group-containing organic compound with 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an organic solvent; and reacting activated carboxyl group-containing organic compound with albumin, wherein said carboxyl group-containing organic compound is a cytostatic or an immunosuppressant.

In contrast, Bures generally describes a method for using protein as a carrier of methotrexate for cancer chemotherapy. Moreover, Bures describes reacting albumin with methotrexate in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an aqueous solution (see e.g., page 331, paragraph 10, “Preparation of the HAS-MTX derivative.”)

Sutton generally describes a method for forming microparticles of a water-soluble material, which carry a therapeutic or diagnostic agent.

Neither Bures nor Sutton teaches or suggests a method for modulating a transplantation-associated immune response using a conjugate comprising a carboxyl group-containing organic compound and albumin, wherein said carboxyl group-containing organic compound is a cytostatic or an immunosuppressant, as recited in instant Claim 1. Moreover, neither Bures nor Sutton Bures mentions activating the carboxyl group-containing organic compound with 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an organic solvent, as recited in instant Claim 15.

Accordingly, Applicants respectfully submit that independent Claims 1 and 15 are not anticipated by Bures or Sutton because neither reference discloses each and every element as set forth in these claims. Applicants further submit that Claims 3-8, 10, 12-14 and 17-22 are patentable over Bures or Sutton because they depend from one of Claims 1 and 15, and recite additional patentable subject matter. Therefore, withdrawal of the rejection to Claims 1, 3-8, 10,

12-15 and 17-22 under 35 U.S.C. §102 is respectfully requested. Claims 2, 9, 11 and 16 have been canceled. Rejection to these claims is now moot.

The grounds for this rejection have been obviated and withdrawal of the 35 U.S.C. §102 rejection is respectfully requested.

**Claim Rejections Under 35 § 103(a)**

Claim 19 stands rejected under 35 U.S.C. § 103(a) as being obvious over the Bures for the reasons set forth on page 4 of the Office Action, and as being obvious over Sutton (U.S. Patent No. 5,993,805) for the reasons set forth on page 5 of the Office Action. Claim 20 stands rejected under 35 U.S.C. § 103(a) as being obvious over Sutton (U.S. Patent No. 5,993,805) for the reasons set forth on pages 5-6 of the Office Action. Applicant respectfully traverses the rejection.

To establish a prima facie case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F. 2d981, 180 USPQ 580 (CCPA, 1974).

Claims 19 and 20 depend from Claim 15. As discussed above, independent Claim 15, as amended, is directed to a method for preparing a conjugate comprising a carboxyl group-containing organic compound and albumin, said method comprising: activating said carboxyl group-containing organic compound with 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an organic solvent; and reacting activated carboxyl group-containing organic compound with albumin, wherein said carboxyl group-containing organic compound is a cytostatic or an immunosuppressant.

Further, as discussed above, neither Bures nor Sutton Bures teaches or suggests activating the carboxyl group-containing organic compound with 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an organic solvent, as recited in Claim 15. In fact, Bures teaches away from the claimed invention by disclosing reacting albumin with methotrexate in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbonyldiimide in an aqueous solution (see e.g., page 331, paragraph 10, “Preparation of the HAS-MTX derivative.”)

Therefore, Claim 15 is not obvious over Bures or Sutton because these reference fail to teach or suggest all the claim limitations. Accordingly, Claim 19 and 20 are not obvious over Bures or Sutton because they depend from Claim 15 and recite additional patentable subject matter. For instance, neither Bures nor Sutton teaches or suggests reacting methotrexate with albumin at a methotrexate:albumin molar ratio of 10:1 to 1:10, as recited in Claim 19. Furthermore, Bures and Sutton do not mention activating the carboxyl group-containing organic compound with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide in an anhydrous organic solvent by heating, as recited in Claim 20.

In view of the foregoing, Bures and Sutton do not support a *prima facie* case of obviousness. The grounds for this rejection have been obviated and withdrawal of the 35 U.S.C. §103 rejection is respectfully requested.

## CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to contact Applicant's counsel, Ping Wang, M.D. (Reg. No. 48,328), at 202.842.0217.

Respectfully submitted,

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### Attachments:

Copy of the signed Declaration in German language  
English translation of Declaration  
Statement stating that the translation is accurate